UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/578,693	05/26/2000	Masaya Yamanouchi	0020-4710P	9841

2292 7590 05/01/2009

BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER	
COOK, LISA V	

ART UNIT	PAPER NUMBER
1641	

NOTIFICATION DATE	DELIVERY MODE
05/01/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte MASAYA YAMANOUCHI, AKIO HONDA, HIROMI HASE, TAKESHI SUGAYA, and KENJIRO KIMURA

Appeal 2008-6229
Application 09/578,693
Technology Center 1600

Decided:[1] April 29, 2009

Before TONI R. SCHEINER, DONALD E. ADAMS, and ERIC GRIMES, *Administrative Patent Judges*.

GRIMES, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims 2, 4, 6, 9, 16-19, 21-24, and 27, all of the pending claims, which are directed to a

---

[1] The two-month time period for filing an appeal or commencing a civil action, as recited in 37 C.F.R. § 1.304, begins to run from the decided date shown on this page of the decision. The time period does not run from the Mail Date (paper delivery) or Notification Date (electronic delivery).

method for diagnosis or prognosis of kidney disease. The Examiner has rejected the claims as obvious.. We have jurisdiction under 35 U.S.C. § 6(b). We reverse.

STATEMENT OF THE CASE

The Specification discloses that "fatty acid binding protein (FABP) is known to be a group of proteins of a molecular weight of about 15 kilodalton, existing in cytosol, and having an ability of binding to a fatty acid . . . but the detailed physiological activities of these proteins have not been clarified yet" (Spec. 2: 8-16). "There have been known at least seven molecules of FABP such as liver-type (L-FABP), intestine-type (I-FABP), heart muscle-type (H-FABP)," etc. (*id.* at 2: 16-18).

The Specification discloses "a method for examination, which is useful in diagnosing kidney diseases . . . [based on] a relation between the existence of fatty acid binding proteins in kidney tissue and the prognosis of kidney diseases" (*id.* at 4: 15-20). The Specification discloses that in humans and other non-rodents, "when the existing amount of L-FABP in the specimen collected from kidney tissues is lower than that of the normal kidney, then it is estimated that there is a high risk for bad prognosis" (*id.* at 19: 23 to 20: 1). When the specimen is urine, "[o]n the other hand . . . , it is estimated that prognosis is expected to be good when the existing level of L-FABP is low" because a high level of L-FABP in urine would indicate leakage from the kidney tissue into the urine (*id.* at 20: 5-14).

Claims 16 and 24, the only independent claims, read as follows:

16. A method for diagnosis or prognosis of a kidney disease in human, which comprises the steps of:

(a) preparing a specimen collected from a human;

(b) detecting liver-type fatty acid binding protein contained in said specimen; and
(c) diagnosing or prognosing the kidney disease based on the test result of the detection in (b), wherein said specimen is kidney tissue or urine.

24. A method for diagnosing the progression of kidney disease in a patient suffering therefrom, comprising the steps of:
(a) preparing a specimen collected from said patient;
(b) assaying for liver-type fatty acid binding protein contained in said specimen; and
(c) diagnosing the progression of the kidney disease based on the test result of the detection in (b), wherein said specimen is kidney tissue or urine.

The claims stand rejected under 35 U.S.C. § 103(a) as follows:

• Claims 2, 4, 6, 16-18, 22-24, and 27 as obvious in view of Gorski,[2] Maatman,[3] and Simon[4] (Ans. 4);

• Claim 9 as obvious in view of Gorski, Maatman, Simon, and Kimura[5] (Ans. 6); and

• Claims 19 and 21 as obvious in view of Gorski, Maatman, Simon, and Galaske[6] (Ans. 7).

OBVIOUSNESS

Issue

The Examiner has rejected most of the pending claims as obvious in view of Gorski, Maatman, and Simon (Ans. 4). The Examiner finds that

---

[2] Gorski et al., 43 Clinical Chemistry 193-195 (1997).
[3] Maatman et al., 288 Biochem. J. 285-290 (1992).
[4] Simon et al., 272 J. Biol. Chem. 10652-10663 (1997).
[5] Kimura et al., 266 J. Biol. Chem. 5963-5972 (1991).
[6] Galaske et al., 375 Pflügers Arch. Eur. J. Physiol. 269-277 (1978).

Gorski discloses "evaluating the increased concentration of fatty acid binding protein (FABP) concentrations in plasma samples of patients with chronic renal failure," but does not teach detection of liver-type FABP (*id.*).

The Examiner finds that Maatman teaches that L-FABP is expressed in kidney and "speculates that it is utilized in nephrotoxicity" (*id.* at 5), and that Simon teaches that "the liver fatty acid binding protein functions to suppress expression in the proximal nephron (kidney tissue)" (*id.*). The Examiner concludes that it would have been obvious "to use the liver-type fatty acid binding protein as taught by Maatmann [sic] et al., having proven function in the kidney (nephron) as taught by Simon et al. to detect the specific kidney diseases relating to FABP in the method of Gorski et al." (*id.*).

Appellants contend that the claimed method would not have been obvious in view of the cited references at least because "there exists no motivation to replace the H-FABP of Gorski with the L-FABP of Maatman or Simon. . . . [T]here is no indication that H-FABP and L-FABP are similar or equivalent. . . . [and] Maatman only provides mere speculation as to the function of L-FABP." (App. Br. 12-13.)

The issue with respect to this rejection is: Does the evidence of record support the Examiner's conclusion that Maatman and Simon would have suggested, to a person of ordinary skill in the art, modifying Gorski's method to measure L-FABP?

Findings of Fact

1. Gorski discloses that "[h]eart and skeletal muscles contain the same type of FABP," specifically H-FABP (Gorski 193, right col.).

2. A person of ordinary skill in the art would understand Gorski's references to "FABP" to mean heart-type FABP (H-FABP).

3. Gorski discloses that the "concentration of FABP in the plasma of healthy persons is relatively low . . . [but] FABP is released from the heart early after the onset of infarction, whereafter its plasma concentration increases manyfold" (*id.*).

4. Gorski discloses that "[i]ncreased excretion of FABP in urine also occurs after infarction" (*id.*).

5. Gorski discloses that "recent studies indicate the usefulness of the plasma FABP concentration as an early biochemical marker for myocardial infarction diagnosis" (*id.*).

6. Gorski discloses that "to interpret properly the values of plasma FABP concentration, one has to take into account not only its source and rate of release into plasma but also its elimination from plasma. It is obvious that any change in the clearance rate of FABP would affect its plasma concentration, and thus may lead to erroneous interpretation." (*Id.* at 193, right col. to 194, left col.)

7. Gorski discloses that "[l]ow-molecular-mass proteins such as FABP and myoglobin are cleared mostly by the kidney" (*id.* at 194, left col.).

8. Gorski discloses that a patient with myocardial infarction and renal insufficiency had been reported to show elevated plasma FABP 25 hours after infarction, whereas in patients with normal kidney function FABP level normalizes about 10 hours after infarction (*id.*).

9. Gorski compared plasma FABP and myoglobin levels in patients with renal failure (but no myocardial infarction) to those in healthy control patients (*id.* at 194, Table 1).

10. Gorski discloses that the data "show that plasma FABP concentration is markedly increased in patients with chronic renal failure and normal heart function, similar to that found for myoglobin" (*id.* at 194, right col.).

11. Gorski concludes that the

> data indicate that in patients with chronic renal failure the plasma concentrations of the biochemical markers FABP and myoglobin each are markedly increased. Thus, caution must be taken when using these marker proteins for early diagnosis of myocardial infarction, in case of renal insufficiency, as the preinfarct plasma concentration is very likely to be already high.

(*Id.* at 195, left col.)

12. Maatman discloses that both liver-type (L-FABP) and heart-type (H-FABP) fatty acid binding proteins are expressed in human kidney cells (Maatman, abstract).

13. Maatman states:

> We can only speculate on the physiological relevance of the two FABP types in kidney. The liver-type FABP binds various ligands and may be involved in the renal excretion of exogenous and endogenous metabolites. The liver-type FABP also binds some drugs, and may in this way prevent nephrotoxicity. The heart-type FABP only binds fatty acids and seems to be involved in lipid metabolism.

(*Id.* at 289, right col., reference citations omitted.)

14. Maatman states that the "significance of the occurrence in kidney of two FABP types with different ligand specificities and cellular distributions requires further investigation" (*id.*).

15. Simon discloses a "35-nucleotide sequence in the liver fatty acid-binding protein gene (*Fabpl*) . . . that interacts with nuclear proteins present in adult mouse liver, kidney, stomach, small intestine, and colon. The binding site consists of a direct heptad repeat (*TTCTG*NN*TT*) separated by five nucleotides." (Simon, abstract.)

16. Simon discloses that the "*in vivo* functions mediated by the repeats were determined by comparing the expression of four *Fabpl*/human growth hormone fusion genes in multiple pedigrees of adult transgenic mice" (*id.*).

17. Simon discloses that the "heptad repeat functions to suppress expression in tubular epithelial cells of the proximal nephron," among other tissues (*id.*).

18. Simon concludes that the

> heptad repeat represents a target for identifying transcription factors that regulate gene expression between gut and renal epithelia and that also regulate the differentiation program of the intestine's principal epithelial lineage as a function of its location along the duodenal-colonic axis. Finally, the *Fabpl* regulatory elements . . . should be useful for delivering a variety of gene products throughout the colonic epithelium of transgenic mice.

(*Id.*)

Principles of Law

A "patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. . . . [I]t can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007).

"We must still be careful not to allow hindsight reconstruction of references to reach the claimed invention without any explanation as to how or why the references would be combined to produce the claimed invention." *Innogenetics, N.V. v. Abbott Labs.*, 512 F.3d 1363, 1374 n.3 (Fed. Cir. 2008).

Analysis

Gorski discloses that the plasma (or urine) concentration of heart-type fatty acid binding protein (H-FABP) can be useful in diagnosing myocardial infarction. Gorski also teaches that the kidneys clear H-FABP from the bloodstream and, as a result, plasma H-FABP concentration is elevated in patients with renal failure. Gorski teaches that clinicians must be cautious in using H-FABP to diagnose myocardial infarction, because patients with renal failure will show high plasma concentrations of H-FABP even in the absence of myocardial infarction.

Gorski does not teach that the concentration of H-FABP in plasma or urine can be used to diagnose renal failure or other kidney disease.

Maatman discloses that kidney tissues express both H-FABP and liver-type fatty acid binding protein (L-FABP). Maatman speculates that L-

FABP might bind certain drugs and thereby prevent them from killing kidney cells (nephrotoxicity). Maatman does not, however, disclose any relationship between any kidney disease and the amount of L-FABP in kidney tissue, plasma, or urine.

Simon teaches that a 35-nucleotide sequence from the L-FABP gene interacts with nuclear proteins and suppresses expression of an L-FABP/ human growth hormone fusion protein in, among other cells, the tubular epithelial cells of the proximal nephron of the kidney. Simon suggests that the L-FABP-derived sequence would be useful for identifying transcription factors with certain properties and for expressing foreign genes in the colonic epithelium of transgenic mice. Simon does not disclose any relationship between any kidney disease and the amount of L-FABP in kidney tissue, plasma, or urine.

Thus, none of the references cited by the Examiner discloses that the amount of L-FABP, in any type of patient specimen, is related to either the presence or severity of kidney disease in a patient. The Examiner has not adequately shown that Gorski's method of diagnosing myocardial infarction by measuring H-FABP, combined with the disclosures of Maatman and Simon, would have made obvious the claimed method of determining a diagnosis or prognosis of kidney disease by measuring L-FABP.

The Examiner also rejected claim 9 as obvious in view of Gorski, Maatman, Simon, and Kimura (Ans. 6) and rejected claims 19 and 21 as obvious in view of Gorski, Maatman, Simon, and Galaske (Ans. 7). In both rejections, the Examiner relied on Gorski, Maatman, and Simon for the teachings discussed above, and concluded that Kimura or Galaske would

have suggested the limitations of the rejected dependent claims. The Examiner pointed to nothing in either Kimura or Galaske to remedy the deficiency, discussed above, in the combination of Gorski, Maatman, and Simon. We therefore reverse the rejections of claims 9, 19, and 21 for the reasons discussed above.

CONCLUSION OF LAW

The evidence of record does not support the Examiner's conclusion that Maatman and Simon would have suggested, to a person of ordinary skill in the art, modifying Gorski's method to measure L-FABP.

SUMMARY

We reverse the rejection of claims 2, 4, 6, 16-18, 22-24, and 27 as obvious in view of Gorski, Maatman, and Simon; the rejection of claim 9 as obvious in view of Gorski, Maatman, Simon, and Kimura; and the rejection of claims 19 and 21 as obvious in view of Gorski, Maatman, Simon, and Galaske.

REVERSED

Ssc:

BIRCH STEWART KOLASCH & BIRCH
P.O. BOX 747
FALLS CHURCH, VA 22040-0747